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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,144	01/30/2004	Tibor Keler	CDJ-301	9318

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EXAMINER	
KIM, YUNSOO	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/769,144	KELER ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 33-59 are pending.

Claims 50-59 have been added in the amendment filed 6/29/06 and thus the claims 56-57 are not original claims.

2. In view of Applicants' amendments to claims and specification, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 41-44 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody that binds to an antigen presenting cell (APC) wherein the antibody consisting of human heavy chain variable region comprising of FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 and a human light chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 or any human heavy chain or light chain variable region consisting of SEQ ID NO: 4 and 8, or CDRs identified as in SEQ ID NOs: 13-18, does not reasonably provide enablement for any antibody comprising the conservative sequence modifications thereof SEQ ID NOs as disclosed in claims 41-44 and for the reasons set forth in the office action mailed 12/29/05.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant's arguments filed 6/29/06 have been fully considered but they were not persuasive.

Applicants' traversed the rejection based on the presently amended claims encompass the conservative sequence modifications and the conservative sequence modifications are well known in the art.

As discussed in the office action mailed 12/29/05, given the established unpredictability of the art, the instant specification would require a significant guidance to how to make and use the conservative sequence modification thereof SEQ ID NOs: 4, 8, 13-18. It is unlikely that the generic modified molecular conjugates encompassed by the claims would function for their intended use. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al. (Proc Natl Acad Sci USA 1982 Vol 79 page 1979, of record). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function.

The specification does not provide any guidance to which amino acid in CDR retains the binding characteristics or which conservative sequence modification thereof affect the binding characteristics of the antibody containing the claimed amino acid sequence.

To summarize, reasonable correlation must exist between the scope or the claims and scope of the enablement set forth. In view of the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breath of the claims, it would take undue trials and errors to practice the claimed invention.

5. Claims 41-44 are rejected under 35.U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the claimed invention for the reasons set forth in the office action mailed 12/29/05.

Applicant is in possession of an antibody that binds to an antigen presenting cell (APC) wherein the antibody consisting of human heavy chain variable region comprising of FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 and a human light chain variable region comprising FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4 or any human heavy chain or light chain variable region consisting of SEQ ID NO: 4 and 8, or CDRs identified as in SEQ ID NOs: 13-18, however, applicant is not in possession of any antibody comprising the "conservative modifications thereof" SEQ ID NOs disclosed in claims 41-44.

Applicant's arguments filed 6/29/06 have been fully considered but they were not persuasive.

Applicants' traversed the rejection based on the presently amended claims encompass the conservative sequence modifications and the conservative sequence modifications are well known in the art.

There is insufficient written description encompassing "conservative sequence modifications thereof" SEQ ID NOs: 4, 8, 13-18 as recited in claims 41-44 because any amino acid sequence of different chemical or physical properties of amino acid is not set forth in the specification as filed, commensurate in scope with the claimed invention. Therefore, Applicant does not possess the scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

However, there are 56 non-polar amino acids out of 107 amino acids in SEQ ID NO:8 and the conservative sequence modification encompasses $9.7x\ 10^{13}$ possible combinations of amino acid sequences of SEQ ID NO:8 alone without any other possible combinations of light chain into consideration. Therefore, Applicant does not possess the scope of claimed invention. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use.

Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601,1606 (CAFC 1993).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 33-37, 39-45 and 47-59 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO 01/85798 A2 (IDS reference, of record) for the reasons set forth in the office action mailed 12/29/05.

Applicant's arguments filed 6/29/06 have been fully considered but they were not persuasive.

Applicants' traversed the rejection based on that the prior art had not shown the CTL responses mediated by both MHC Class I and Class II pathways.

As discussed in the office action mailed 12/29/05, the '798 publication teaches a method of enhancing the immune response by an human monoclonal antibody to antigen presenting cell such as dendritic cells conjugated to tumor antigen (p. 5-6, 54-55, in particular), *in vivo* and *ex vivo* internalization of antigen by APC, immune response mediated by MHC-I/II complexes, antibody being Fab and use of immunostimulatory cytokines such as GM-CSF as an adjuvant (p. 5-6, 26, 38-41, 56-58, claims 16, 23-27, 32, 38-42, in particular).

The '798 publication further teaches the antibody mediates cytotoxic T cell response (p. 6, 35-36, in particular) and antibody comprising SEQ ID NOs: 4 and 8 (example 2, SEQ ID NOs: 2 and 4, in particular). As the SEQ ID NOs: 4 and 8 encompass the CDRs identified as in SEQ ID NOs: 13-18, the reference teaching meets the claimed limitation.

Claim 33 now recites that the monoclonal antibody binds to human e mannose receptor and the '798 further encompasses the monoclonal antibody binds to human mannose receptor (p. 26, in particular).

The identical immune conjugate comprising an antigen and a monoclonal antibody binds to human mannose receptor via the identical method of contacting (e.g. *in vivo* and *ex vivo* internalization of antigen by APC), the mechanism of inducing the cytotoxic T cell response by both MHC Class I and Class II pathways or CD4+ and CD8+ are inherent property of the immune conjugate comprising an antigen and a monoclonal antibody binds to human mannose receptor. Therefore, reference teachings anticipate the claimed invention.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 33, 38 and 46 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/85798 (IDS reference, of record) in view of U.S. Pat. No. 5,869,057 (IDS reference, of record) for the reasons set forth in the office action mailed 12/29/05.

Applicant's arguments filed 6/29/06 have been fully considered but they were not persuasive.

Applicants' traversed the rejection based on that the '798 publication is not prior art and the combination is not obvious.

The teachings of the '798 publication have been discussed, supra.

The '798 publication does not teach the use of βhCG as an antigen.

However, the '057 patent teaches the use of βhCG as an antigen (i.e. detectable on the 74 cancer cell lines, col. 3, lines 40-50, col. 5, lines 32-60, in particular) as well as its capacity to present antigen to CD4+ cells (col. 3, lines 25-30, in particular). The '057 patent further teaches that the βhCG is a general tumor antigen which could be using immunization against βhCG as an antimetastasis treatment.

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to substitute the antigen with βhCG as taught by the '057 patent in a method of enhancing an CTL response taught by the '798 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the βhCG is a well characterized tumor antigen as well as its capacity to present antigen to CD4+ cells and the use in immunization as taught by the '057 patent (col. 3, and 5 in particular).

From the teachings of references, it would have been obvious to one of the ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In light of the discussion above, the '798 publication is a prior art and the combination of teachings remain obvious.

10. The following new ground of rejection is necessitated by the Applicants' amendment filed 6/29/06.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 33-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification as file does not provide a written description for the phrase "human **macrophage** mannose receptor". The specification on p. 3 lines 25-30 discloses "human mannose receptor expressed **on APC**". The scope of the claims 33-59 does not commensurate with the scope of the specification.

13. No claims are allowable.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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September 13, 2006

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